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Scandium Ion-Promoted Reduction of Heterocyclic N═N Double Bond. Hydride Transfer vs Electron Transfer

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Abstract: Hydride transfer from 10-methyl-9,10-dihydroacridine ($AcrH_2$) to 3,6-diphenyl-1,2,4,5-tetrazine (Ph_2Tz), which contains a N═N double bond, occurs efficiently in the presence of $Sc(OTf)_3$ (OTf = OSO_2CF_3) in deaerated acetonitrile (MeCN) at 298 K, whereas no reaction occurs in the absence of Sc^{3+}. The observed second-order rate constant (k_{obs}) increases with increasing Sc^{3+} concentration to approach a limited value. When $AcrH_2$ is replaced by the dideuterated compound ($AcrD_2$), the rate of Sc^{3+}-promoted hydride transfer exhibits the same primary kinetic isotope effect ($k_H/k_D = 5.2 \pm 0.2$), irrespective of Sc^{3+} concentration. Scandium ion also promotes an electron transfer from CoTPP (TPP^{2-} = tetraphenylporphyrin dianion) and 10,10′-dimethyl-9,9′-biacridine [$(AcrH)_2$] to Ph_2Tz, whereas no electron transfer from CoTPP or $(AcrH)_2$ to Ph_2Tz occurs in the absence of Sc^{3+}. In each case, the observed second-order rate constant of electron transfer (k_{et}) shows a first-order dependence on [Sc^{3+}] at low concentrations and a second-order dependence at higher concentrations. Such dependence of k_{et} on [Sc^{3+}] is ascribed to formation of 1:1 and 1:2 complexes between $Ph_2Tz^{\bullet-}$ and Sc^{3+} at the low and high concentrations of Sc^{3+}, respectively, which results in acceleration of the rate of electron transfer. The formation of 1:2 complex has been confirmed by the ESR spectrum in which the hyperfine structure is different from that of free $Ph_2Tz^{\bullet-}$. The 1:2 complex formation results in the saturated kinetic dependence of k_{obs} on [Sc^{3+}] for the Sc^{3+}-promoted hydride transfer, which proceeds via Sc^{3+}-promoted electron transfer from $AcrH_2$ to Ph_2Tz, followed by proton transfer from $AcrH_2^{\bullet+}$ to the 1:1 $Ph_2Tz^{\bullet-}-Sc^{3+}$ complex and the subsequent facile electron transfer from $AcrH^{\bullet}$ to $Ph_2TzH^{\bullet}$. The effects of counteranions on the Sc^{3+}-promoted electron transfer and hydride transfer reactions are also reported.

Introduction

Nicotinamide adenine dinucleotide (NADH) is the most important electron source in biological redox reactions, providing a hydride ion that is equivalent to two electrons and a proton. Mechanisms of hydride transfer reactions of NADH analogues with hydride acceptors such as carbonyl compounds and organic cations have been extensively studied chemically[1−8] or electrochemically.[9,10] The effects of metal ions on hydride transfer reactions from NADH analogues to substrates have particularly

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attracted considerable interest in relation to the catalytic role of metal ions in the redox reactions of nicotinamide coenzymes in the native enzymatic system.[1−4,11,12] Metal ions acting as Lewis acids are known to promote electron-transfer reactions, where metal ions bind to the product radical anions produced in the electron-transfer reactions.[13−16] Both thermal and photochemical redox reactions that would otherwise be unlikely to occur are made possible to proceed efficiently by the catalysis of metal ions on the electron-transfer steps.[13−16] Among metal ions, rare-earth metal ions have particularly attracted considerable attention as much more effective Lewis acids than divalent metal ions such as Mg^{2+} and Zn^{2+} in various carbon−carbon bond-forming reactions due to the strong affinity to carbonyl oxygen.[17−19] In particular, scandium ion (Sc^{3+}) has recently been reported to accelerate electron-transfer reduction of *p*-benzoquinone derivatives much more efficiently than any other metal ion, including lanthanide ions.[20] The reactions of NADH analogues with *p*-benzoquinone derivatives, which are normally good hydride acceptors, are also accelerated most remarkably by Sc^{3+}.[20] In this case, however, efficient [2 + 3] cycloaddition reactions of NADH analogues with *p*-benzoquinone derivatives rather than the hydride transfer reactions occur in the presence of scandium triflate [$Sc(OTf)_3$] in MeCN.[20] Moreover, there has so far been no report on the metal ion-promoted hydride transfer from an NADH analogue to hydride acceptors other than carbonyl compounds, which would be difficult to reduce without the metal ion. The effects of counterions on the metal ion-promoted electron transfer or hydride transfer have yet to be examined.

We report herein that hydride transfer from an NADH analogue to 3,6-diphenyl-1,2,4,5-tetrazine (Ph_2Tz), which would otherwise be difficult to reduce,[21] occurs efficiently in the presence of $Sc(OTf)_3$ ($OTf = OSO_2CF_3$) in MeCN. 1,2,4,5-Tetrazines containing a N═N double bond are valuable electron-deficient 4π components that have been utilized in Diels−Alder reactions with inverse electron demanding, making a large variety of valuable compounds available.[22−24] The kinetic analysis of the Sc^{3+}-promoted hydride transfer reactions involving kinetic deuterium isotope effects as compared with the authentic electron-transfer reactions provides valuable information for the Sc^{3+}-promoted electron-transfer step and the subsequent proton-transfer step in the overall hydride transfer reaction. The key intermediate for the Sc^{3+}-promoted reduction of Ph_2Tz is found to be the complex formed between the radical anion of Ph_2Tz and Sc^{3+}, which is detected successfully by ESR spectroscopy in this study. The effects of counterions have also been studied to reveal the relation between the electron transfer and the hydride transfer reactions.

Experimental Section

The standard procedures of experiments including product analysis and kinetic measurements are given in the Supporting Information (S1).

Materials. The preparation of 10-methyl-9,10-dihydroacridine ($AcrH_2$) and the dideuterated compound ($AcrD_2$) was described previously.[4a] The dimeric 1-benzyl-1,4-dihydronicotinamide dimer [$(BNA)_2$] was prepared according to the literature procedure.[25] Cobalt(II) tetraphenylporphyrin (CoTPP) was prepared as given in the literature.[26] 10,10′-Dimethyl-9,9′-biacridine [$(AcrH)_2$] was prepared by the one-electron reduction of 10-methylacridinium perchlorate by hexamethylditin.[27] Scandium triflate [$Sc(OTf)_3$] was prepared by the procedure reported elsewhere.[20] Scandium triflate was characterized by ^{13}C NMR in D_2O as compared with the data for $Yb(OTf)_3$.[28]

1,1,1-Trifluoro-*N*-[(trifluoromethyl)sulfonyl]methanesulfonamide, [$Sc(NTf_2)_3$], was obtained commercially from Aldrich. The scandium salt of tetrakis(pentafluorophenyl)borate [$Sc[B(C_6F_5)_4]_3$] was prepared by the following procedure. A powder form of ion-exchange resin (DOWEX 50WX8-200, 0.5 g) obtained from Ardrich was suspended

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in an aqueous solution of $Sc(OTf)_3$ (1.0 g, 200 mL) and stirred by the magnetic stirrer for 1 day. The isolated Sc^{3+}-exchanged resin was washed with deionized water and dried under vacuum for one night. An aqueous solution of lithium tetrakis(pentafluorophenyl)borate diethyl ether complex (2.9×10^{-2} M, 50 mL) obtained from Tokyo Chemical Industry Co., Ltd. was added dropwise to the glass short column packed with the Sc^{3+}-exchanged resin. The aqueous solution of the scandium borate salt ($Sc[B(C_6F_5)_4]_3$) trickled down the column and was concentrated by the vacuum evaporation followed by drying under vacuum for one night. The white powder of $Sc[B(C_6F_5)_4]_3$ with water of crystallization was identified by Shimadzu TOF mass spectrometer, AXIMA-CFR (see Supporting Information S2). Acetonitrile used as a solvent was purified and dried by the standard procedure.[29] Acetonitrile-d_3 and dimethyl sulfoxide-d_6 were obtained from EURI SO-TOP, CEA, France.

Electrochemical Measurements. Electrochemical measurements were performed on a BAS 100B electrochemical analyzer in deaerated MeCN containing 0.10 M n-$Bu_4N^+ClO_4^-$ (TBAP) as a supporting electrolyte at 298 K. The platinum working electrode was polished with BAS polishing alumina suspension and rinsed with acetone before use. The counter electrode was a platinum wire. The measured potentials were recorded with respect to an $Ag/AgNO_3$ (0.01 M) reference electrode. The second-harmonic alternating current voltammetry (SHACV)[30] measurements of Ph_2Tz in the presence of $Sc(OTf)_3$ were carried out with a BAS 100B electrochemical analyzer in deaerated MeCN containing 0.10 M TBAP as a supporting electrolyte at 298 K. The E^0_{red} values (vs $Ag/AgNO_3$) are converted into those vs SCE by addition of 0.29 V.[31]

ESR Measurements. Ph_2Tz was dissolved in MeCN (1.0×10^{-3} M in 1.0 mL) and purged with argon for 10 min. $Sc(OTf)_3$ (8.8×10^{-2} M in 1.0 mL) and $Sc[B(C_6F_5)_4]_3$ (2.0×10^{-1} M in 1.0 mL) were dissolved in deaerated MeCN. The Ph_2Tz solution (200 μL) and Sc^{3+} solution (200 μL) were introduced into the ESR cell (1.8 mm i.d.) containing $(BNA)_2$ (2.0×10^{-2} M) and mixed by bubbling with Ar gas through a syringe with a long needle. The ESR spectra of the $Ph_2Tz^{\bullet-}-2Sc^{3+}$ complex were recorded on a JEOL JES-RE1XE spectrometer under irradiation of a high-pressure mercury lamp (USH-1005D) focusing at the sample cell in the ESR cavity at 298 K. The ESR spectrum of $Ph_2Tz^{\bullet-}$ was also measured in the absence of $Sc(OTf)_3$ under otherwise the same experimental conditions. The magnitude of modulation was chosen to optimize the resolution and signal-to-noise (S/N) ratio of the observed spectra under nonsaturating microwave power conditions. The g values were calibrated using an Mn^{2+} marker.

Theoretical Calculations. Density functional calculations were performed on a COMPAQ DS20E computer using the spin-restricted B3LYP functional for the open shell molecule.[32] The B3LYP geometry of $Ph_2Tz^{\bullet-}-2H^+$ was determined using the 6-31G(3d,3p) basis set and the Gaussian 98 program.[33] The $\langle S^2 \rangle$ value was determined as 0.761, indicating a good representation of the doublet state.

Results and Discussion

Sc^{3+}-Promoted Hydride Transfer from $AcrH_2$ to Ph_2Tz. Upon addition of $AcrH_2$ (1.7×10^{-3} M) to a deaerated MeCN solution of Ph_2Tz (1.7×10^{-3} M) in the presence of $Sc(OTf)_3$ (1.4×10^{-2} M), hydride transfer from $AcrH_2$ to Ph_2Tz occurs efficiently to yield 10-methylacridinium ion ($AcrH^+$) and dihydrotetrazine (Ph_2TzH_2) in MeCN at 298 K (eq 1, for the product analysis, see Experimental Section).[34–37] As the reaction proceeds, the absorption band due to Ph_2Tz ($\lambda_{max} = 540$ nm) decreases and this is accompanied by the appearance of a new absorption band ($\lambda_{max} = 358$ nm) due to the formation of $AcrH^+$ (Figure 1). In the absence of Sc^{3+}, no reaction has occurred between $AcrH_2$ and Ph_2Tz.

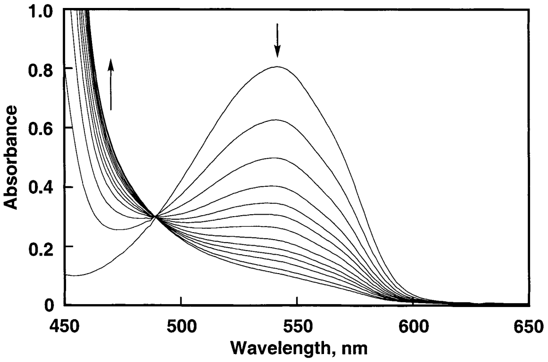
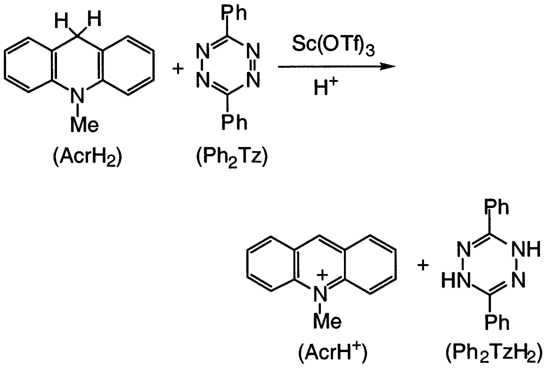


Figure 1. Spectral change in the reaction of $AcrH_2$ (1.7×10^{-3} M) with Ph_2Tz (1.7×10^{-3} M) in the presence of Sc^{3+} (1.4×10^{-2} M) in deaerated MeCN at 298 K (time interval, 400 s).



(1)

The spectral titration in which the absorbance due to Ph_2Tz at $\lambda = 540$ nm is plotted against $[AcrH_2]/[Ph_2Tz]_0$ (see

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(33) Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, J. A., Jr.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Baboul, A. G.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. *Gaussian 98 (Revision A.7)* Gaussian, Inc.; Pittsburgh, PA, 1998.

(34) Formation of Ph_2TzH_2 was confirmed by comparing the ^1H NMR data (see Experimental Section) with the reported values. See: Nagy, J.; Nyitrai, J.; Kolonits, P.; Lempert, K.; Gergely, A.; Párkányi, L.; Kálmán, A. *J. Chem. Soc., Perkin Trans. 1* **1988**, 3267. Three positional isomers (1,4-, 1,2-, and 3,6-isomers) are expected to be formed as dihydro-3,6-diphenyl-1,2,4,5-tetrazine on the basis of the ^1H NMR data (see Experimental Section); however, the 1,4-isomer (eqs 1 and 7) is the most likely candidate, since it was calculated to be thermodynamically more stable than the 1,2- and 3,6-isomer by 6.7 and 28.0 kcal mol^{-1}, respectively at the B3LYP/6-31G* level.

(35) The proton required for formation of Ph_2TzH_2 comes from water contained in MeCN. The acidity of water in the presence of $Sc(OTf)_3$ in acetonitrile-d_3 increases as compared with that in the absence of $Sc(OTf)_3$, as indicated by the low-field shift of ^1H NMR signal due to water.

(36) Since $AcrH_2$ is known to be oxidized by oxygen in the presence of acids in MeCN,[37] oxygen was excluded in the reaction procedure.

(37) Fukuzumi, S.; Chiba, M.; Ishikawa, M.; Ishikawa, K.; Tanaka, T. *J. Chem. Soc., Perkin Trans 2* **1989**, 1417.

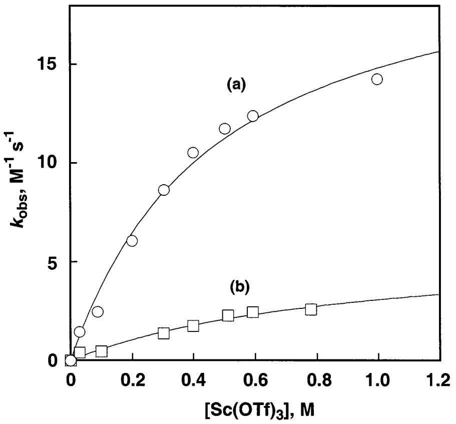


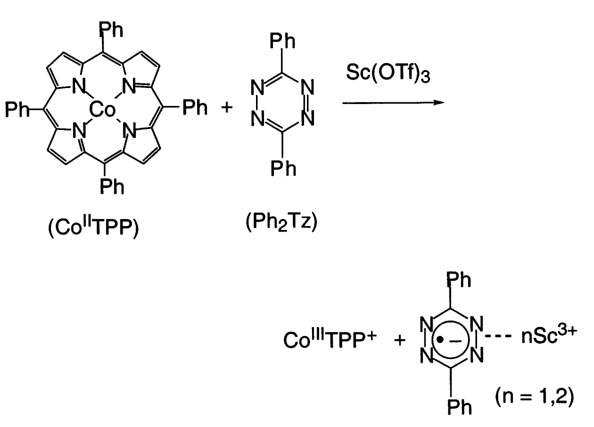
Figure 2. Plots of k_{obs} vs [Sc(OTf)$_3$] for reduction of Ph$_2$Tz by (a) AcrH$_2$ (○, 2.5 × 10^{-4} M) and (b) AcrD$_2$ (□, 2.0 × 10^{-4} M) in the presence of Sc(OTf)$_3$ in deaerated MeCN at 298 K.

Supporting Information S3) confirms the stoichiometry in eq 1, where 1 equiv of AcrH$_2$ reacts with 1 equiv of Ph$_2$Tz to yield 1 equiv of AcrH$^+$ and Ph$_2$TzH$_2$.

The rates of Sc^{3+}-promoted hydride transfer reaction were determined by monitoring the appearance of absorbance due to AcrH$^+$ (λ_{max} = 358 nm, ϵ_{max} = 1.9 × 10^4 M^{-1} cm^{-1}). The rates obeyed pseudo-first-order kinetics in the presence of large excess Ph$_2$Tz and Sc^{3+} relative to the concentration of AcrH$_2$ (see Supporting Information S5). The pseudo-first-order rate constant (k_1) increases proportionally with Ph$_2$Tz concentration (see Supporting Information S5). Thus, the rate exhibits a second-order kinetics showing a first-order dependence on each reactant concentration.

The dependence of the observed second-order rate constant (k_{obs}) on [Sc^{3+}] was examined for the Sc^{3+}-promoted hydride transfer reaction at various concentrations of Sc^{3+}. The k_{obs} value increases with an increase in [Sc^{3+}] to approach a limited value, as shown in Figure 2a. When AcrH$_2$ is replaced by the dideuterated compound (AcrD$_2$), a large kinetic primary isotope effect is observed as shown in Figure 2b.

Sc^{3+}-Promoted Electron-Transfer Reduction of Ph$_2$Tz. When AcrH$_2$ is replaced by a one-electron reductant such as CoTPP (TPP^{2-} = tetraphenylporphyrin dianion), electron transfer from CoTPP to Ph$_2$Tz also occurs efficiently in the presence of Sc(OTf)$_3$ in MeCN (eq 2), whereas no electron



(2)

transfer from CoTPP to Ph$_2$Tz occurred without Sc(OTf)$_3$. The electron-transfer rates obeyed a second-order kinetics, showing a first-order dependence on each reactant concentration. The dependence of the observed electron-transfer rate constant (k_{et}) on [Sc^{3+}] was also examined for electron transfer from CoTPP to Ph$_2$Tz at various concentrations of Sc^{3+}. The results are quite different from those of the hydride transfer reaction, as shown in Figure 3a, where the k_{et} value increases with increasing [Sc^{3+}] to exhibit a mixture of a first-order and second-order dependence on [Sc^{3+}] (vide infra).

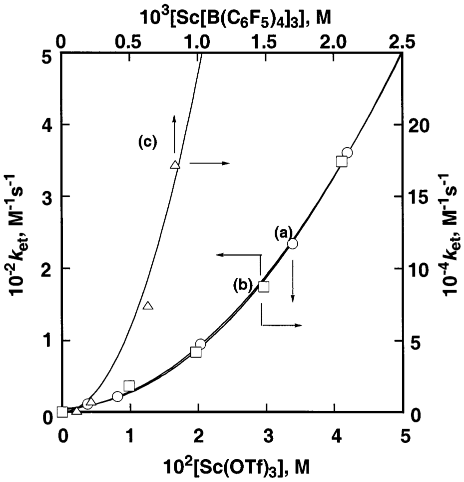


Figure 3. Plots of k_{et} vs [Sc(OTf)$_3$] for electron transfer from (a) CoTPP- (○, 2.1 × 10^{-6} M) and (b) (AcrH)$_2$ (□, 8.4 × 10^{-5} M) to Ph$_2$Tz in the presence of Sc(OTf)$_3$, and (c) for electron transfer from CoTPP (△, 2.1 × 10^{-6} M) to Ph$_2$Tz in the presence of Sc[B(C$_6$F$_5$)$_4$]$_3$ in MeCN at 298 K.

It was confirmed that there was no interaction between Ph$_2$Tz and Sc^{3+}, as indicated by the lack of spectral change of Ph$_2$Tz in the presence of Sc^{3+}.[38] In such a case, the acceleration of electron transfer from CoTPP to Ph$_2$Tz is ascribed to the complexation of Sc^{3+} with Ph$_2$Tz$^{\bullet-}$. The contribution of the second-order dependence of k_{et} on [Sc^{3+}] in Figure 2a suggests that Ph$_2$Tz$^{\bullet-}$ may form not only a 1:1 complex (n = 1 in eq 2) but also a 1:2 complex (n = 2 in eq 2) with Sc^{3+}. The complex formation of Ph$_2$Tz$^{\bullet-}$ and Sc^{3+} should result in the positive shift of the one-electron reduction potential of Ph$_2$Tz (E_{red}), and the Nernst equation may be given by eq 3,

$$E_{red} = E^0_{red} + (2.3RT/F)\log K_1[\mathrm{Sc}^{3+}](1 + K_2[\mathrm{Sc}^{3+}]) \qquad (3)$$

where E^0_{red} is the one-electron reduction potential of Ph$_2$Tz in the absence of Sc^{3+}, and K_1 and K_2 are the formation constants for the 1:1 and 1:2 complexes between Ph$_2$Tz$^{\bullet-}$ and Sc^{3+}, respectively. Since Sc^{3+} has no effect on the oxidation potential of CoTPP, the free energy change of electron transfer from CoTPP to Ph$_2$Tz in the presence of Sc^{3+} (ΔG_{et}) can be expressed by eq 4,

$$\Delta G_{et} = \Delta G^0_{et} - (2.3RT)\log(K_1[\mathrm{Sc}^{3+}] + K_1K_2[\mathrm{Sc}^{3+}]^2) \qquad (4)$$

where ΔG^0_{et} is the free energy change in the absence of Sc^{3+}.

Thus, electron transfer from CoTPP to Ph$_2$Tz becomes more favorable energetically with an increase in concentration of Sc^{3+}. If such a change in the energetics is directly reflected in the

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(38) No complex formation between Ph$_2$Tz and Sc^{3+} in acetonitrile was confirmed by the ^{1}H and ^{13}C NMR titration. ^{1}H NMR (CD$_3$CN) in the absence of Sc(OTf)$_3$: δ 8.60 (dd, J = 8.0, 1.5 Hz, 4H), 7.68 (m, 6H). ^{1}H NMR (CD$_3$CN) in the presence of 0.38 M Sc(OTf)$_3$: δ 8.60 (dd, J = 8.0, 1.5 Hz, 4H), 7.68 (m, 6H). ^{13}C NMR (CD$_3$CN) in the absence of Sc(OTf)$_3$: δ 128.56 (s), 128.75 (s), 130.11 (s), 130.61 (s), 164.97 (s). ^{13}C NMR (CD$_3$CN) in the presence of 0.07 M Sc(OTf)$_3$: δ 128.56 (s), 128.75 (s), 130.11 (s), 130.61 (s), 164.97 (s).

Table 1. Rate Constants (k_0K_1) of Sc^{3+}-Promoted Electron Transfer from CoTPP and $(AcrH)_2$ to Ph_2Tz and the Formation Constants (K_2) of the $Ph_2Tz^{\bullet -}-2Sc^{3+}$ Complexes in Deaerated MeCN at 298 K

electron donor	k_0K_1,[a] $M^{-2}\,s^{-1}$	K_2,[a] M^{-1}
CoTPP	9.4×10^5	8.2×10
$(AcrH)_2$	1.8×10^3	8.5×10

[a] Determined from the dependence of k_{obs} on $[Sc^{3+}]$ based on eq 6. The experimental error is 10%.

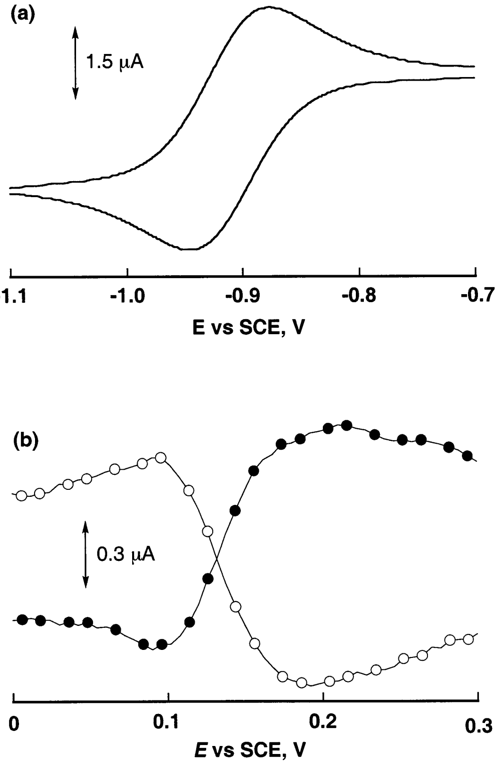


Figure 4. (a) Cyclic voltammogram of Ph_2Tz (1.0×10^{-3} M) in deaerated MeCN containing 0.10 M TBAP with Pt electrode at 298 K and (b) SHACV of Ph_2Tz (1.0×10^{-3} M) in the presence of $Sc(OTf)_3$ (4.1×10^{-3} M) in deaerated MeCN containing 0.10 M TBAP with Pt electrode at 298 K.

transition state of electron transfer, the dependence of the observed rate constant of electron transfer (k_{et}) on $[Sc^{3+}]$ is derived from eq 4, as given by eq 5,

$$k_{et} = k_0K_1([Sc^{3+}] + K_2[Sc^{3+}]^2) \tag{5}$$

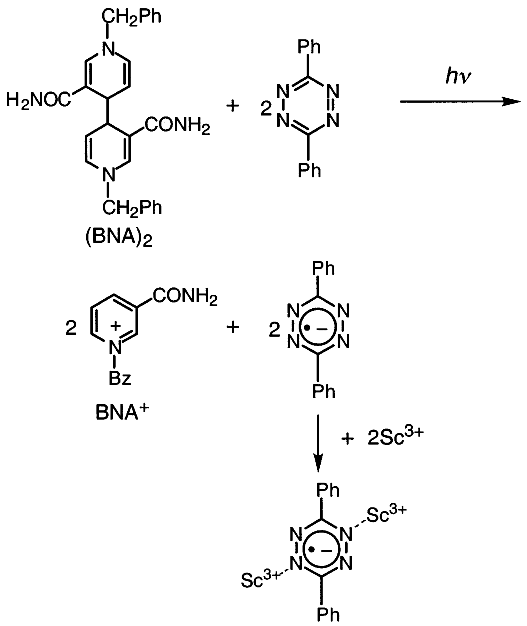
where k_0 is the rate constant in the absence of Sc^{3+}. From eq 5 is derived eq 6,

$$k_{et}/[Sc^{3+}] = k_0K_1(1 + K_2[Sc^{3+}]) \tag{6}$$

the validity of which is confirmed by the linear plot of $k_{et}/[Sc^{3+}]$ vs $[Sc^{3+}]$ for the Sc^{3+}-promoted electron transfer from CoTPP to Ph_2Tz (see Supporting Information S6). From the slope and intercept is obtained the K_2 value which is listed in Table 1 together with the k_0K_1 value. The solid lines in Figure 3 are drawn on the basis of eq 5 with these parameters.

The positive shift of E_{red} caused by the complexation of $Ph_2Tz^{\bullet -}$ with Sc^{3+} was verified by the electrochemical measurements. The cyclic voltammogram of Ph_2Tz exhibits a reversible redox wave, as shown in Figure 4a. The one-electron reduction potential of Ph_2Tz is determined from the half-wave potential as −0.91 V (vs SCE). The addition of $Sc(OTf)_3$ (4.1×10^{-3} M) to an MeCN solution of Ph_2Tz results in a largely positive shift of the one-electron reduction potential (+1.04 V), as shown in Figure 4b, where the second harmonic ac voltammogram affords the one-electron reduction potential (+0.13 V).[39,40]

Scheme 1



Detection of the $Ph_2Tz^{\bullet -}-2Sc^{3+}$ Complex. The 1:2 complex formation between $Ph_2Tz^{\bullet -}$ and Sc^{3+} has been confirmed by the observation of the ESR spectrum of the $Ph_2Tz^{\bullet -}-2Sc^{3+}$ complex, which is compared with that of $Ph_2Tz^{\bullet -}$ (vide infra). The $Ph_2Tz^{\bullet -}$ was produced by photoinduced electron transfer from dimeric 1-benzyl-1,4-dihydronicotinamide $[(BNA)_2]$[41] to Ph_2Tz in MeCN at 233 K (Scheme 1). The $(BNA)_2$ is known to act as a unique electron donor to produce the radical anions of electron acceptors.[42] The ESR spectrum of $Ph_2Tz^{\bullet -}$ thus obtained under photoirradiation exhibits nine hyperfine lines as shown in Figure 5a, indicating that four nitrogens are equivalent [a(4N) = 5.1 G]. The addition of $Sc(OTf)_3$ (4.4×10^{-2} M) to the $(BNA)_2-Ph_2Tz$ system results in a drastic change in the hyperfine pattern of $Ph_2Tz^{\bullet -}$ due to the complexation with Sc^{3+} (Scheme 1), as shown in Figure 5b. The ESR spectrum is well-reproduced by the computer simulation spectrum with the hfc values of a(2N) = 6.6, 5.0 G and a(6H) = 5.0 G (Figure 5c). The four equivalent nitrogens of $Ph_2Tz^{\bullet -}$ are split into two sets of two equivalent nitrogens due to the complexation with two Sc^{3+} ions. The absence of superhyperfine lines due to the scandium nucleus indicates that the interaction between $Ph_2Tz^{\bullet -}$ and two Sc^{3+} ions is largely electrostatic rather than covalent. The complexation of $Ph_2Tz^{\bullet -}$ with two Sc^{3+} ions

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(39) The cyclic voltammogram of Ph_2Tz in the presence of $Sc(OTf)_3$ shows an irreversible cathodic wave due to the instability of the $Ph_2Tz^{\bullet -}-Sc^{3+}$ complex. Although the one-electron reduction potential determined by SHACV[30] may involve uncertainty due to the instability of the $Ph_2Tz^{\bullet -}-Sc^{3+}$ complex, the observed large positive shift as compared to that in the absence of Sc^{3+} is unmistakable.

(40) An even larger positive shift (+2.02 V) of the reversible one-electron reduction potential of a naphthoquinone derivative, determined by CV, has been reported to be caused by the complexation of the radical anion with Sc^{3+} (7.0 mM) in MeCN. See: Fukuzumi, S.; Okamoto, K.; Imahori, H. *Angew. Chem., Int. Ed.* **2002**, *41*, 620. For other examples, see ref 14.

(41) Patz, M.; Kuwahara, Y.; Suenobu, T.; Fukuzumi, S. *Chem. Lett.* **1997**, 567.

(42) Fukuzumi, S.; Suenobu, T.; Patz, M.; Hirasaka, T.; Itoh, S.; Fujitsuka, M.; Ito, O. *J. Am. Chem. Soc.* **1998**, *120*, 8060.

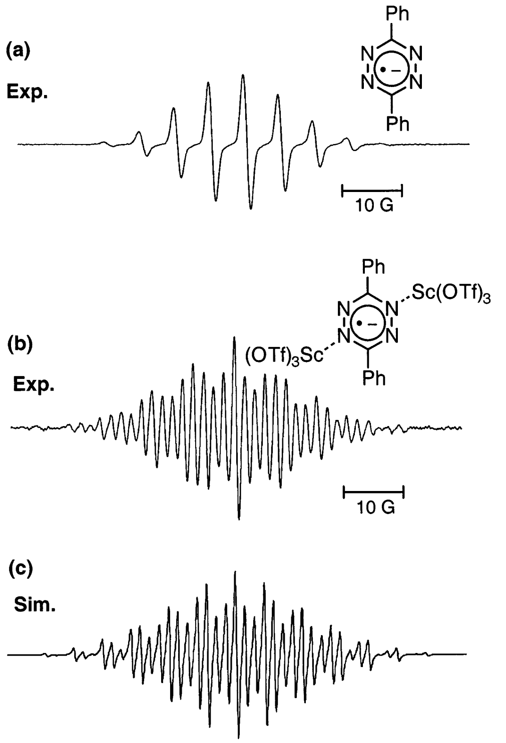
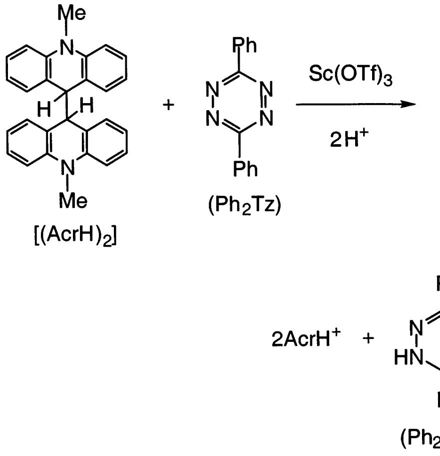


Figure 5. ESR spectra of an MeCN solution containing $(BNA)_2$ (2.0×10^{-2} M) and Ph_2Tz (5.0×10^{-4} M) in the absence (a) and presence (b) of $Sc(OTf)_3$ (4.4×10^{-2} M) under irradiation with a high-pressure mercury lamp at 233 K. (c) Computer-simulated spectrum for condition b with $g = 2.0041$, $a(2N^1) = 6.6$ G, $a(2N^2) = 5.0$ G, $a(6H) = 5.0$ G, and $\Delta H_{msl} = 0.40$ G.

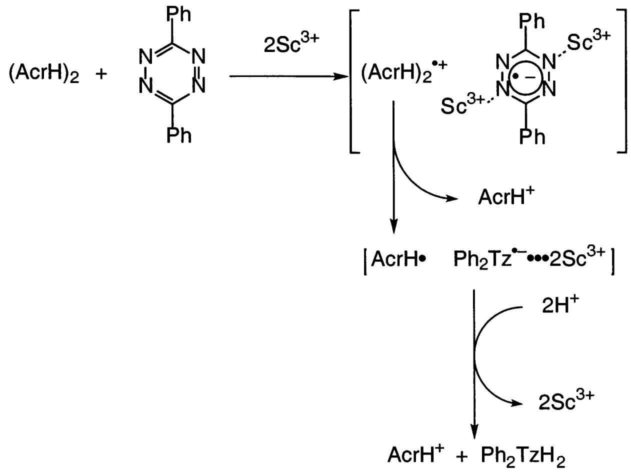
also results in the structural change such that the phenyl group becomes coplanar with the heterocycle ring when the hyperfine lines due to six equivalent protons appear due to the spin delocalization on the phenyl group in the Sc^{3+} complex. Such coplanarity in the Sc^{3+} complex is supported by the B3LYP theoretical calculation of the protonated species $Ph_2Tz^{\bullet-}-2H^+$ (see Supporting Information S7).

Electron Transfer vs Hydride Transfer. The acridine dimer, 10,10′-dimethyl-9,9′-biacridine [$(AcrH)_2$], is known to act as an electron donor, in contrast with the case of the monomer, $AcrH_2$, which is a hydride donor.[43,44] Electron transfer from $(AcrH)_2$ to Ph_2Tz occurs efficiently in the presence of $Sc(OTf)_3$ in MeCN at 298 K to yield $AcrH^+$ and Ph_2TzH_2 (eq 7), which are the same as the products of the Sc^{3+}-promoted hydride transfer reaction from $AcrH_2$ to Ph_2Tz (eq 1).[35] The spectral titration (see Supporting Information S8) confirms the stoichiometry in eq 7, where 1 equiv of $(AcrH)_2$ reacts with 1 equiv of Ph_2Tz to yield 2 equiv of $AcrH^+$ and Ph_2TzH_2. In this case, the initial Sc^{3+}-promoted electron transfer from $(AcrH)_2$ to Ph_2Tz is followed by the facile C−C bond cleavage to give $AcrH^+$ and $AcrH^\bullet$ (Scheme 2). Since $AcrH^\bullet$ (E^0_{ox} vs SCE = −0.46 V)[4e] is much stronger reductant than $(AcrH)_2$ (E^0_{ox} vs SCE = 0.62 V),[43] the rapid electron transfer from $AcrH^\bullet$ to the $Ph_2Tz^{\bullet-}-2Sc^{3+}$ complex occurs to yield the final products, $AcrH^+$ and Ph_2TzH_2 after replacement of Sc^{3+} by H^+ (Scheme 2).[35]



(7)

Scheme 2



The rates of Sc^{3+}-promoted electron transfer from $(AcrH)_2$ to Ph_2Tz were determined by monitoring the appearance of absorbance due to $AcrH^+$ as in the case of the hydride transfer from $AcrH_2$ to Ph_2Tz. However, the dependence of the observed second-order rate constant (k_{et}) on [Sc^{3+}] is different from that for the Sc^{3+}-promoted hydride transfer reaction in Figure 2a, but it is virtually the same as that for the Sc^{3+}-promoted electron transfer from CoTPP to Ph_2Tz (Figure 3a): the k_{et} value increases linearly with [Sc^{3+}] to show a first-order dependence on [Sc^{3+}] at low concentrations, changing to a second-order dependence at high concentrations (Figure 3b). The same linear plot of k_{et}/[Sc^{3+}] vs [Sc^{3+}] is applied for the Sc^{3+}-promoted electron transfer from $(AcrH)_2$ to Ph_2Tz to afford the K_2 value as 85 M^{-1} (Figure 4b). This value agrees with the K_2 value (82 M^{-1}) derived from the Sc^{3+}-promoted electron transfer from CoTPP to Ph_2Tz (Figure 4a). Such an agreement indicates that the rate-determining step for the two-electron reduction of Ph_2Tz by $(AcrH)_2$ is indeed the Sc^{3+}-promoted electron transfer from $(AcrH)_2$ to Ph_2Tz (Scheme 2).

The saturated dependence of k_{obs} with respect to [Sc^{3+}] for the Sc^{3+}-promoted hydride transfer from $AcrH_2$ to Ph_2Tz (Figure 2a) normally results from the complex formation between Ph_2Tz and Sc^{3+}, which enhances the electrophilicity of Ph_2Tz to accelerate the hydride transfer reaction. However, as noted earlier, there was no interaction between Ph_2Tz and Sc^{3+}. Only the one-electron reduced species, i.e., $Ph_2Tz^{\bullet-}$, can form the complex with Sc^{3+} (vide supra). In such a case, the dependence

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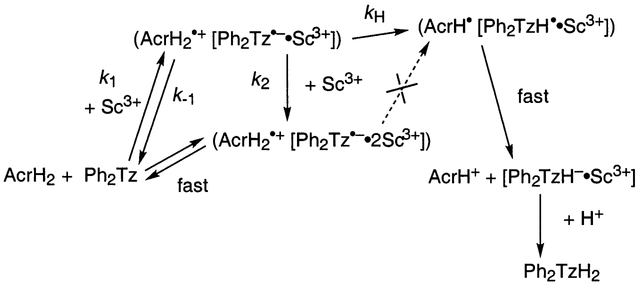
(43) Fukuzumi, S.; Tokuda, Y. *J. Phys. Chem.* **1992**, *96*, 8409.

(44) The acridine dimer [$(AcrH)_2$] is employed instead of $(BNA)_2$, since $(AcrH)_2$ has no interaction with Sc^{3+}, whereas the carbonyl oxygen of [$(BNA)_2$] forms a complex with Sc^{3+}.[20] The electron-transfer oxidation mechanism of $(AcrH)_2$ is similar to that of $(BNA)_2$, although the oxidation potentials of $(AcrH)_2$ and $AcrH^\bullet$ are much higher than those of $(BNA)_2$ and $BNA^\bullet$.[42,43]

Scheme 3



of k_{obs} on [Sc^{3+}] and the observed primary kinetic isotope effects in Figure 2 can be best explained by Scheme 3 (vide infra).

Electron transfer from $AcrH_2$ to Ph_2Tz is highly endergonic, judging from the E^0_{ox} value of $AcrH_2$ (0.81 V)[4e] and the E^0_{red} value of Ph_2Tz (−0.91 V), and no reaction occurs between $AcrH_2$ and Ph_2Tz. In the presence of $Sc(OTf)_3$ (4.1×10^{-3} M), however, the reduction potential of Ph_2Tz is shifted to +0.13 V when electron transfer from $AcrH_2$ to Ph_2Tz becomes much less endergonic as compared with electron transfer without $Sc(OTf)_3$. Although the free energy change of electron transfer is still positive, electron transfer is followed by proton transfer from $AcrH_2^{\bullet+}$ to the $Ph_2Tz^{\bullet-}-Sc^{3+}$ complex and the subsequent electron transfer from $AcrH^{\bullet}$ to $Ph_2TzH^{\bullet}$ may be highly exergonic to yield the final products, $AcrH^+$ and Ph_2TzH_2 (Scheme 3). The overall reaction is exergonic and the hydride transfer reaction occurs irreversibly when the observed second-order rate constant (k_{obs}) may be given by eq 8,

$$k_{obs} = k_H(k_1/k_{-1})[Sc^{3+}] \tag{8}$$

which predicts that the k_{obs} value increases linearly with [Sc^{3+}]. At high concentrations of Sc^{3+}, however, the $Ph_2Tz^{\bullet-}-Sc^{3+}$ complex is converted to the 1:2 complex $Ph_2Tz^{\bullet-}-2Sc^{3+}$, the basicity of which is reduced significantly as compared to the 1:1 complex, as shown in Scheme 3. In such a case, proton transfer from $AcrH_2^{\bullet+}$ to the $Ph_2Tz^{\bullet-}-2Sc^{3+}$ complex is retarded when the overall rate would reach a limited value. Under such experimental conditions, k_{obs} is given by eq 9,

$$k_{obs} = k_1k_H[Sc^{3+}]/(k_{-1} + k_H + k_2[Sc^{3+}]) \tag{9}$$

which predicts that the k_{obs} value exhibits a saturated dependence with respect to [Sc^{3+}]. According to eq 9, there would be no primary kinetic isotope effect under the conditions such that $k_H \gg k_{-1} + k_2[Sc^{3+}]$ when $k_{obs} = k_1[Sc^{3+}]$. On the other hand, the primary kinetic isotope effect would be the same independent of [Sc^{3+}] under the conditions such that $k_H \ll k_{-1} + k_2[Sc^{3+}]$. The latter case is consistent with the experimental observation in Figure 2. Under such conditions, eq 9 is reduced to eq 10,

$$k_{obs} = k_1k_H[Sc^{3+}]/(k_{-1} + k_2[Sc^{3+}]) \tag{10}$$

which agrees with the saturated dependence of k_{obs} on [Sc^{3+}] in Figure 2. Such a saturated dependence of k_{obs} on [Sc^{3+}] can be expressed by a double-reciprocal plot of k_{obs}^{-1} on $[Sc^{3+}]^{-1}$ according to eq 11.

$$k_{obs}^{-1} = (k_{-1}/k_1k_H)[Sc^{3+}]^{-1} + (k_2/k_1k_H) \tag{11}$$

From the slope and intercept of the linear plots (See Supporting Information S9) are obtained the k_{-1}/k_1k_H and k_2/k_1k_H values for $AcrH_2$ and k_{-1}/k_1k_D and k_2/k_1k_D values for $AcrD_2$. The solid lines in Figure 2 are drawn on the basis of eq 10 with these parameters. The k_H/k_D value obtained from the ratio of the slopes (5.0) agrees with that from the intercepts (5.4).

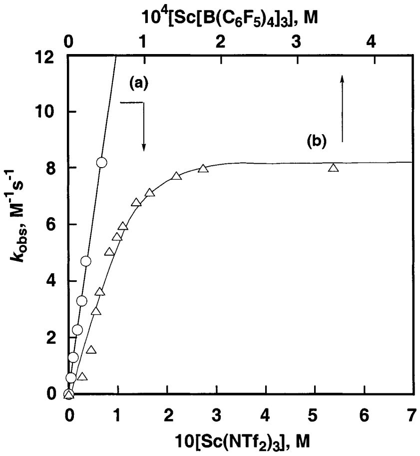


Figure 6. Plots of k_{obs} vs (a) [$Sc(NTf_2)_3$] and (b) [$Sc[B(C_6F_5)_4]_3$] for the reaction of Ph_2Tz with $AcrH_2$ (a: 2.5×10^{-4} M, b: 4.9×10^{-6} M) in the presence of $Sc(NTf_2)_3$ and $Sc[B(C_6F_5)_4]_3$ in deaerated MeCN at 298 K.

Effects of Counteranions. The Lewis acidity of Sc^{3+} is expected to be regulated by counterions. When $Sc(OTf)_3$ is replaced by the weaker Lewis acid, $Sc(NTf_2)_3$, the k_2 value is expected to be smaller, but the k_{-1} value may be larger than the value of $Sc(OTf)_3$. In such a case, $k_{-1} \gg k_2[Sc^{3+}]$ when eq 10 is reduced to eq 8. This expectation is confirmed as shown in Figure 6a, where the k_{obs} value of the $Sc(NTf_2)_3$-promoted hydride transfer from $AcrH_2$ to Ph_2Tz increases linearly with [$Sc(NTf_2)_3$] up to large concentrations, where the k_{obs} value of the $Sc(OTf)_3$-promoted reaction exhibits the saturated dependence (Figure 2). Conversely, when $Sc(OTf)_3$ is replaced by a stronger Lewis acid, $Sc[B(C_6F_5)_4]_3$, the k_{obs} value reaches a constant value at the much smaller concentration, as shown in Figure 6b, as compared to the k_{obs} value of the $Sc(OTf)_3$-promoted reaction. The use of such a bulky counteranion $B(C_6F_5)_4^-$ results in the weaker interaction between Sc^{3+} and the counteranion, thereby increasing the Lewis acidity of Sc^{3+}. The weak nucleophilicity of $B(C_6F_5)_4^-$ has been well-documented.[45]

The stronger Lewis acidity of $Sc[B(C_6F_5)_4]_3$ than $Sc(OTf)_3$ is confirmed by the much higher reactivity in the $Sc[B(C_6F_5)_4]_3$-promoted electron transfer from CoTPP to Ph_2Tz, as shown in Figure 3c. The ESR spectrum of the $Ph_2Tz^{\bullet-}-2Sc[B(C_6F_5)_4]_3$ complex is observed under photoirradiation of the $(BNA)_2-Ph_2Tz$ system in the presence of $Sc[B(C_6F_5)_4]_3$ (0.1 M) in MeCN at 233 K, as shown in Figure 7a, which is different from the spectrum of the $Ph_2Tz^{\bullet-}-2Sc(OTf)_3$ complex in Figure 5b. The ESR spectrum is well-reproduced by the computer simulation spectrum with the hfc values of $a(2N) = 6.1$, 4.7 G and $a(6H) = 4.7$ G. These hfc values are smaller than those of the $Ph_2Tz^{\bullet-}-2Sc(OTf)_3$ complex, since the stronger interaction between $Ph_2Tz^{\bullet-}$ and $Sc[B(C_6F_5)_4]_3$ results in more delocalization of spin to the carbon atoms.

In conclusion, Sc^{3+} can promote both electron transfer from CoTPP and $(AcrH)_2$ to Ph_2Tz and hydride transfer from $AcrH_2$

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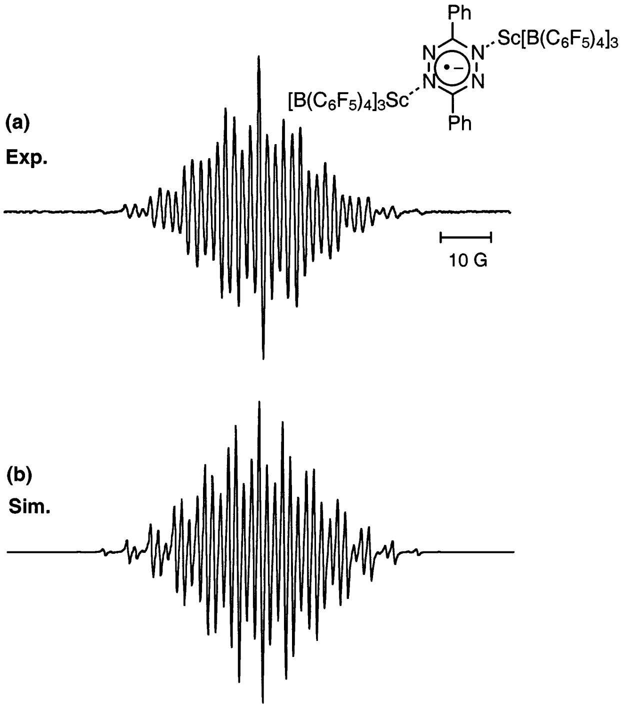

Figure 7. (a) ESR spectrum of an MeCN solution containing (BNA)$_2$ (2.0 $\times$ 10^{-2} M) and Ph$_2$Tz (5.0 $\times$ 10^{-4} M) in the presence of Sc[B(C$_6$F$_5$)$_4$]$_3$ (1.0 $\times$ 10^{-1} M) under irradiation with a high-pressure mercury lamp at 233 K. (b) Computer-simulated spectrum with $g = 2.0039$, $a(2\mathrm{N}^1) = 6.1$ G, $a(2\mathrm{N}^2) = 4.7$ G, $a(6\mathrm{H}) = 4.7$ G, and $\Delta H_{\mathrm{msl}} = 0.40$ G.

to Ph$_2$Tz. The hydride transfer reaction proceeds via the Sc^{3+}-promoted electron transfer from AcrH$_2$ to Ph$_2$Tz, followed by proton transfer and electron transfer. The overall reactivity is regulated by the initial electron transfer and the subsequent proton-transfer processes, in which the formation of a 1:2 complex between Ph$_2$Tz$^{\bullet-}$ and Sc^{3+} accelerates the electron transfer but decelerates the proton-transfer process. Such accelerating and decelerating effects of Sc^{3+} are controlled by the counterions, which alter the Lewis acidity of Sc^{3+}. Thus, the balance between the accelerating effects of Sc^{3+} on the electron-transfer step and the decelerating effects on the subsequent proton-transfer step is of importance to control the overall reactivity of the hydride transfer reaction of NADH analogues.

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Supporting Information Available: Supporting Experimental Section (S1), TOF/MS spectrum for Sc[B(C$_6$F$_5$)$_4$]$_3$·12H$_2$O (S2), UV−vis spectral change in the reaction between Ph$_2$Tz and AcrH$_2$ (S3), time course of the absorption change and the first-order plot (S4), plots of pseudo-first-order rate constant vs [Ph$_2$Tz] (S5), plots of k_{et}/[Sc(OTf)$_3$] vs [Sc(OTf)$_3$] (S6), optimized structure of Ph$_2$Tz$^{\bullet-}$−2H$^+$ (S7), UV−vis spectral change in the reaction between Ph$_2$Tz and (AcrH)$_2$ (S8), and plots of $k_{\mathrm{obs}}{}^{-1}$ vs [Ph$_2$Tz]$^{-1}$ (S9). This material is available free of charge via the Internet at http://pubs.acs.org.

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