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Spiropyran as a Selective, Sensitive, and Reproducible Cyanide Anion Receptor

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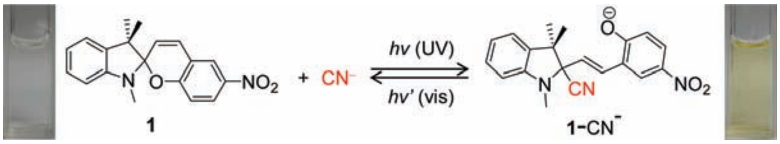
ABSTRACT



A spiropyran derivative (1) behaves as a selective and sensitive cyanide anion receptor in aqueous media under UV irradiation. The receptor can be reproduced just by irradiation with visible light.

The cyanide anion (CN^-) is an anion extremely toxic to living organisms.[1] It strongly binds to cytochrome-c and disrupts the mitochondrial electron-transport chain, leading to decreased oxidative metabolism and oxygen utilization.[2] The maximum permissive level of cyanide in drinking water is therefore set at 1.9 μM by the World Health Organization (WHO).[3] The use of cyanide salts, however, is widespread, particularly in gold mining, electroplating, and metallurgy.[4] Despite increasing levels of monitoring, accidental release of CN^- to the environment does occur. There is thus a strong need for CN^--selective receptors. Several receptors have been proposed, but many of these rely on a hydrogen-bonding motif and act only in organic media.[5] To overcome this limitation, reaction-based CN^- receptors have been proposed;[6−8] however, many of these display relatively poor selectivity[6] and a high detection limit (>1.9 μM)[7] in aqueous media. There are only seven reports of CN^- receptors with high selectivity and sensitivity in aqueous media.[8] These receptors, however, suffer from the biggest problem; they react with CN^- irreversibly and cannot be reused for further analysis.

Spiropyran derivatives belong to a class of organic photochromes that have been studied extensively for application in optical switches[9] and memories.[10] These dyes are converted to the colored merocyanine (MC) form upon

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(1) (a) Koenig, R. *Science* **2000**, *287*, 1737–1738. (b) Baud, F. *Hum. Exp. Toxicol.* **2007**, *26*, 191–201.

(2) Camerino, P. W.; King, T. E. *J. Biol. Chem.* **1966**, *241*, 970–979.

(3) *Guidelines for Drinking-Water Quality*; World Health Organization: Geneva, 1996.

(4) (a) Young, C.; Tidwell, L.; Anderson, C. *Cyanide: Social, Industrial and Economic Aspects*: Minerals, Metals, and Materials Society: Warrendale, 2001. (b) *Ullman's Encyclopedia of Industrial Chemistry*, 6th ed.; Wiley-VCH: New York 1999.

(5) For example, see: (a) Miyaji, H.; Sessler, J. L. *Angew. Chem., Int. Ed.* **2001**, *40*, 154–157. (b) Anzenbacher, P. Jr.; Tyson, D. S.; Jursíková, K.; Castellano, F. N. *J. Am. Chem. Soc.* **2002**, *124*, 6232–6233. (c) Chung, Y. M.; Raman, B.; Kim, D.-S.; Ahn, K. H. *Chem. Commun.* **2006**, 186–188.

(6) For example, see: (a) Badugu, R.; Lakowicz, J. R.; Geddes, C. D. *Anal. Chim. Acta* **2004**, *522*, 9–17. (b) Badugu, R.; Lakowicz, J. R.; Geddes, C. D. *Dyes Pigm.* **2005**, *64*, 49–55. (c) Badugu, R.; Lakowicz, J. R.; Geddes, C. D. *J. Am. Chem. Soc.* **2005**, *127*, 3635–3641. (d) Lou, X.; Zhang, L.; Qin, J.; Li, Z. *Chem. Commun.* **2008**, 5848–5850.

(7) For example, see: (a) García, F.; García, J. M.; García-Acosta, B.; Martínez-Máñez, R.; Sancenón, F.; Soto, J. *Chem. Commun.* **2005**, 2790–2792. (b) Ros-Lis, J. V.; Martínez-Máñez, R.; Soto, J. *Chem. Commun.* **2005**, 5260–5262. (c) Hudnall, T. W.; Gabbaï, F. P. *J. Am. Chem. Soc.* **2007**, *129*, 11978–11986.

(8) (a) Chow, C.-F.; Lam, M. H. W.; Wong, W.-Y. *Inorg. Chem.* **2004**, *43*, 8387–8393. (b) Jin, W. J.; Fernández-Argüelles, M. T.; Costa-Fernández, J. M.; Pereiro, R.; Sanz-Medel, A. *Chem. Commun.* **2005**, 883–885. (c) Tomasulo, M.; Raymo, F. M. *Org. Lett.* **2005**, *7*, 4633–4636. (d) Yang, Y.-K.; Tae, J. *Org. Lett.* **2006**, *8*, 5721–5723. (e) Tomasulo, M.; Sortino, S.; White, A. J. P.; Raymo, F. M. *J. Org. Chem.* **2006**, *71*, 744–753. (f) Ganesh, V.; Sanz, M. P. C.; Mareque-Rivas, J. C. *Chem. Commun.* **2007**, 5010–5012. (g) Cho, D.-G.; Kim, J. H.; Sessler, J. L. *J. Am. Chem. Soc.* **2008**, *130*, 12163–12167.

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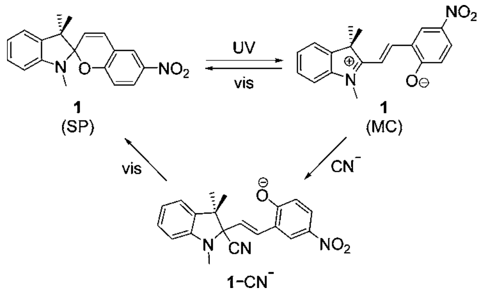
UV irradiation but revert to the colorless spirocyclic (SP) form upon visible light irradiation.[11] Some spiropyran derivatives have been proposed for optical sensing of several analytes, such as cations,[12] nucleobases,[13] amino acids,[14] and DNA.[15] There is, however, no report of a spiropyran-based anion receptor.

Here, we report that a spiropyran derivative behaves as a selective and sensitive CN$^-$ receptor in aqueous media (Scheme 1). A simple, popular, and easily preparable *N*-methylated spiropyran derivative (**1**)[11] shows a CN$^-$-selective absorption band under UV irradiation via a nucleophilic addition of CN$^-$ to **1** (**1**−CN$^-$ adduct formation). This allows quantitative determination of very low levels of CN$^-$ (>1.7 μM). In addition, the receptor can be reproduced just by irradiation with visible light to the **1**−CN$^-$ adduct without any additives.

Scheme 1. Structure Change of **1** in the Presence of CN$^-$ under UV or Visible Light Irradiation



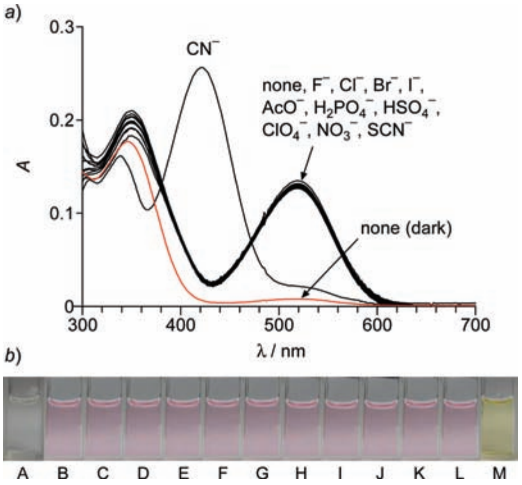


Figure 1. (a) Absorption spectra of 1 (20 μM) measured with 50 equiv of respective anions (as a *n*-Bu$_4$N$^+$ salt) in a water/MeCN mixture (1/1 v/v; CHES 100 mM, pH 9.3) under UV irradiation (334 nm) at 25 °C. The spectra were obtained after stirring the solution containing **1** and each anion for 30 min with UV irradiation. The red spectrum is obtained without anion in the dark. (b) Photographs of the solutions (A) without anion (dark), (B) without anion, (C) F$^-$, (D) Cl$^-$, (E) Br$^-$, (F) I$^-$, (G) AcO$^-$, (H) H$_2$PO$_4^-$, (I) HSO$_4^-$, (J) ClO$_4^-$, (K) NO$_3^-$, (L) SCN$^-$, and (M) CN$^-$.

Figure 1a shows absorption spectra of **1**[16] (20 μM) measured in a buffered water/MeCN mixture (1/1 v/v; CHES 100 mM, pH 9.3) with 50 equiv of respective anions. As shown by the red line, without anion and UV irradiation, **1** shows almost no absorption in the visible region. Upon UV irradiation (334 nm), **1** exhibits a distinctive absorption band centered at 519 nm, assigned to the generation of MC form,[11] with the photostationary state attained after 2 min irradiation. Addition of anions, except for CN$^-$, to the solution under UV irradiation does not show a spectral change. In contrast, addition of CN$^-$ leads to a decrease in the 519 nm MC band, along with an appearance of a blue-shifted band at 421 nm. The spectral change of **1** upon CN$^-$ addition occurs within 25 min under UV irradiation (Figure S1, Supporting Information[16]). As shown in Figure 1b, the solutions obtained under UV irradiation without anion (B) or with other anions (C−L) show a pink color, whereas CN$^-$ addition (M) creates an obvious yellow color. This suggests that **1** allows selective CN$^-$ detection. The CN$^-$-induced spectral change is unaffected by other anions (Figure S2, Supporting Information[16]), indicating that **1** can detect CN$^-$ selectively even in the presence of other anions.

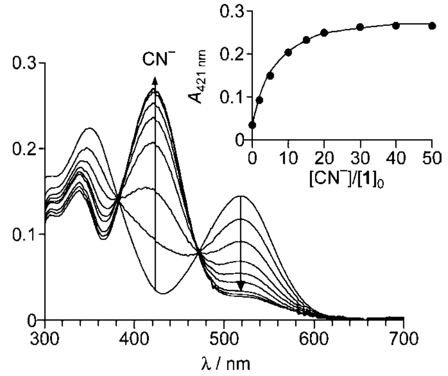


Figure 2. Absorption titration of **1** (20 μM) with CN$^-$ in water/MeCN (1/1 v/v; CHES 100 mM, pH 9.3) under UV irradiation at 25 °C. Each spectrum was obtained after stirring the solution for 30 min with UV irradiation. (Inset) Change in absorbance at 421 nm. The line is the nonlinear fitting curve obtained assuming a 1:1 association between **1** and CN$^-$.[16]

As shown in Figure 2, titration of **1** with CN$^-$ under UV irradiation leads to a decrease in the 519 nm MC band, associated with the 421 nm band increase. The isosbestic points at 382 and 472 nm suggest that the reaction of **1** with CN$^-$ produces a single component. Nonlinear fitting of the data (inset) reveals that **1** reacts with CN$^-$ in a 1:1 stoichiometry with the association constant 9.8×10^3 M^{-1}. The 1:1 reaction is confirmed by ESI-MS (Figure S3, Supporting Information[16]); a MeCN solution containing **1** and CN$^-$, when irradiated with UV light, shows a peak at *m*/*z* 348.5, assigned to [**1** + CN$^-$] ion.

Quantitative CN$^-$ determination can be carried out by ratiometric analysis. Figure 3 shows change in the ratio of

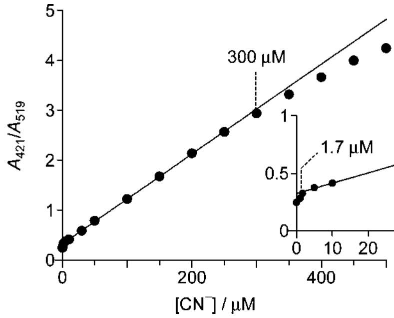


Figure 3. Change in the absorbance ratio (A_{421}/A_{519}) of **1** (10 μM) with CN$^-$ concentration. The titration was performed in water/MeCN (1/1 v/v; CHES 100 mM, pH 9.3) under UV irradiation at 25 °C (Figure S4, Supporting Information[16]). The spectra at each CN$^-$ concentration were obtained after stirring the solution for 30 min under UV irradiation.

the 421 and 519 nm absorbance of **1**. A linear relationship in the range of 1.7−300 μM CN$^-$ indicates that **1** allows accurate CN$^-$ sensing in this concentration range. The detection limit, 1.7 μM, is below the WHO guidelines of drinking water (1.9 μM),[3] suggesting that **1** allows sensitive CN$^-$ detection.

The CN$^-$-induced absorption change is due to the addition of CN$^-$ to the spirocarbon of **1**, leading to a formation of the **1**−CN$^-$ adduct (Scheme 1). ^{1}H NMR spectra of **1** obtained in the dark and after UV irradiation with CN$^-$ confirm this. As shown in Figure 4, chemical shift of some protons of **1** decreases with this process. The biggest change (−0.73 ppm) is observed for the H^g proton in the *ortho* position relative to the phenolate oxygen of **1**, indicating that the reaction of **1** with CN$^-$ produces a spirocycle-opened species.[8e] As reported,[17] olefinic H^i proton of the MC form is magnetically deshielded due to the ring current effect by the adjacent indole moiety and shifts downfield as compared to the SP form. However, in our case, UV irradiation with CN$^-$ leads to upfield shift of H^i (−0.51 ppm). This is because CN$^-$ addition to the spirocarbon of **1** leads to a decrease in electron density of the indole moiety. These data indicate that the reaction of **1** with CN$^-$ under UV irradiation produces the spirocycle-opened **1**−CN$^-$ adduct (Scheme 1).

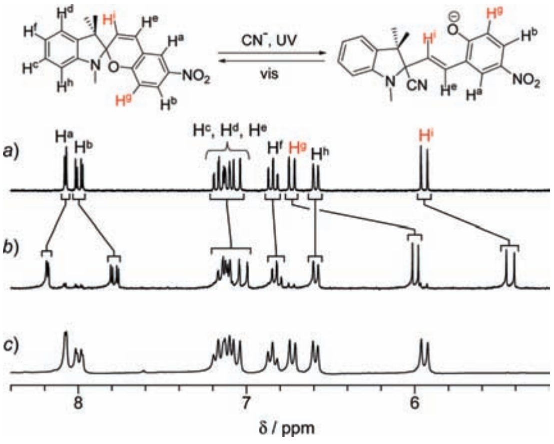


Figure 4. ^{1}H NMR chart (270 MHz, 30 °C, CD$_3$CN) of **1** (5 mM) measured (a) in the dark, (b) after UV irradiation with 10 equiv of CN$^-$, and (c) after three cycles of UV/vis light irradiation with 10 equiv of CN$^-$ (see Figure 7).

The blue-shifted absorption band of the **1**−CN$^-$ adduct compared to the MC form of **1** is due to the localization of π-electrons of the molecule. This is confirmed by ab initio calculations performed within the Gaussian 03 program.[16] The lowest singlet electronic transitions of both **1**(MC) and **1**−CN$^-$ are mainly contributed by a HOMO−LUMO transition, where both transitions have a π,π^* character (Table S1, Supporting Information[16]). As shown in Figure 5, the HOMO−LUMO gap of **1**(MC) is 2.67 eV, whereas the gap of **1**−CN$^-$ is 3.29 eV, suggesting that the adduct has a larger gap than **1**(MC) (Δ0.62 eV). This is explained by electronic configuration of the HOMO and LUMO orbitals. The π-electrons of **1**(MC) are distributed over the entire molecule (Figure 5). In contrast, π-electrons of **1**−CN$^-$ are localized on the *p*-nitrophenolate moiety. This is due to the decrease

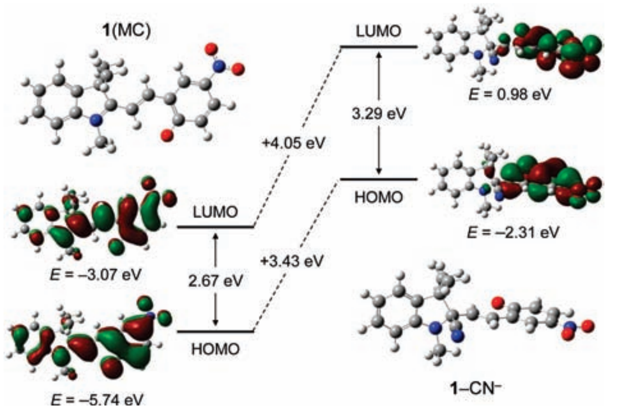


Figure 5. Energy diagrams of HOMO and LUMO orbitals of **1**(MC) and **1**-CN$^-$ calculated at the DFT level using a B3LYP/6-31+G* basis set.

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(9) (a) Raymo, F. M.; Giordani, S. *J. Am. Chem. Soc.* **2001**, *123*, 4651–4652. (b) Zhu, L.; Wu, W.; Zhu, M.-Q.; Han, J. J.; Hurst, J. K.; Li, A. D. Q. *J. Am. Chem. Soc.* **2007**, *129*, 3524–3526.

(10) (a) Nagashima, S.; Murata, M.; Nishihara, H. *Angew. Chem., Int. Ed.* **2006**, *45*, 4298–4301. (b) Tomozaki, K.; Mihara, H. *J. Am. Chem. Soc.* **2007**, *129*, 8345–8352.

(11) (a) Berkovic, G.; Krongauz, V.; Weiss, V. *Chem. Rev.* **2000**, *100*, 1741–1753. (b) Minkin, V. I. *Chem. Rev.* **2004**, *104*, 2751–2776. (c) Raymo, F. M.; Tomasulo, M. *Chem. Soc. Rev.* **2005**, *34*, 327–336.

(12) Inouye, M.; Akamatsu, K.; Nakazumi, H. *J. Am. Chem. Soc.* **1997**, *119*, 9160–9165.

(13) Takase, M.; Inouye, M. *Chem. Commun.* **2001**, 2432–2433.

(14) Shao, N.; Jin, J. Y.; Cheung, S. M.; Yang, R. H.; Chan, W. H.; Mo, T. *Angew. Chem., Int. Ed.* **2006**, *45*, 4944–4948.

(15) Andersson, J.; Li, S.; Lincoln, P.; Andréasson, J. *J. Am. Chem. Soc.* **2008**, *130*, 11836–11837.

(16) See the Supporting Information.

(17) (a) Parker, W. O., Jr.; Hobley, J.; Malatesta, V. *J. Phys. Chem. A* **2002**, *106*, 4028–4031. (b) Machitani, K.; Nakamura, M.; Sakamoto, H.; Ohata, N.; Masuda, H.; Kimura, K. *J. Photochem. Photobiol. A: Chem.* **2008**, *200*, 96–100.

in electron density of the indole moiety by the CN$^-$ addition, which is consistent with the upfield shift of the H^i proton observed by ^{1}H NMR analysis (Figure 4). The lowest singlet transition energy of **1**(MC) is 499 nm (2.48 eV, Table S1, Supporting Information[16]), which is similar to λ_{max} of the **1**(MC) spectrum (519 nm, Figure 2). In contrast, the transition energy of **1**−CN$^-$ (424 nm, 2.92 eV) is much lower than that of **1**(MC) and is similar to λ_{max} of the **1**−CN$^-$ spectrum (421 nm). These closely matched results indicate that the CN$^-$ addition to **1** leads to a localization of the π-electrons; therefore, the adduct requires higher transition energy than **1**(MC), resulting in a blue-shift of the absorption band (Figure 2).

The **1**−CN$^-$ adduct forms via a nucleophilic addition of CN$^-$ to the positively charged spirocarbon[18] of the MC form of **1**, where CN$^-$ does not react with the SP form. This is confirmed by activation energies (E_a) determined by kinetic absorption analysis.[16] The **1**−CN$^-$ formation during the reaction of **1** with an excess amount of CN$^-$ (50 equiv) under UV irradiation is explained by first-order kinetics, with the rate constant 2.44×10^{-3} s^{-1} (25 °C). An Arrhenius plot of the kinetic data reveals that E_a for this reaction is 26.9 kJ mol^{-1} (Figure 6c). In contrast, kinetic analysis in the dark reveals that the rate constant for the reaction between the SP form of **1** and CN$^-$ is 1.75×10^{-5} s^{-1} (25 °C), which is much lower than that for the reaction between **1**(MC) and CN$^-$. In addition, E_a for this reaction is 110.2 kJ mol^{-1} (Figure 6b), which is much higher than E_a for the reaction between **1**(MC) and CN$^-$ and is similar to E_a of the thermal SP→MC isomerization[19] (115.1 kJ mol^{-1}, Figure 6a). These data suggest that the **1**−CN$^-$ adduct forms via reaction of the MC form of **1** with CN$^-$, and hence, UV irradiation is necessary for rapid CN$^-$ sensing by the present receptor.

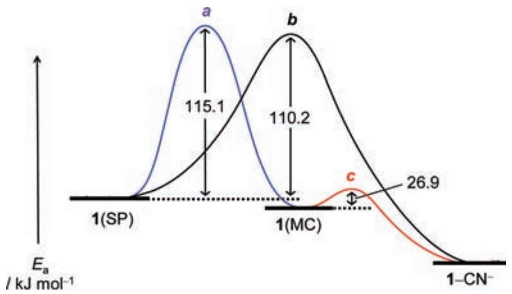

Figure 6. Energy diagrams for respective reactions, (a) **1**(SP) → **1**(MC), (b) **1**(SP) + CN$^-$ → **1**−CN$^-$, and (c) **1**(MC) + CN$^-$ → **1**−CN$^-$, determined by kinetic absorption analysis with 50 equiv of CN$^-$. The kinetic data and Arrhenius plots are shown in Figures S5 and S6 (Supporting Information).[16]

Another significant feature of **1** is that it can be reproduced just by irradiation with visible light. Figure 7 shows the change in 421 nm absorbance of a solution containing **1** and CN$^-$, where UV and visible lights were irradiated sequentially. Visible light irradiation decreases the 421 nm absorption, but sequential UV irradiation regenerates the band. This suggests that the **1**−CN$^-$ adduct, when excited by visible light, successfully reverts to the SP form with a release of CN$^-$ in a way similar to the MC → SP isomerization.[11] Repeated UV and visible light irradiation sequences show almost the same absorbance change. As shown in Figure 4c, the sample recovered after three-cycle irradiations shows an ^{1}H NMR spectrum similar to that for the virgin **1** (Figure 4a). These data clearly indicate that **1** reversibly reacts with CN$^-$ and the process is repeatable without significant degradation of **1**.

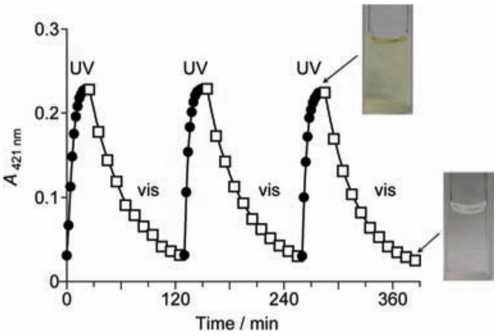

Figure 7. Change in 421 nm absorbance during sequential UV and visible light irradiations of a water/MeCN solution (1/1 v/v; CHES 100 mM, pH 9.3) containing **1** and 50 equiv of CN$^-$ at 25 °C.

In summary, we found that a spiropyran derivative behaves as a selective and sensitive CN$^-$ receptor in aqueous media.[20] The receptor allows accurate sensing of a very low level of CN$^-$ by simple UV−vis analysis. In addition, the receptor is reproduced just by visible light irradiation. Convenient and clean CN$^-$ sensing is realized by applying the basic idea using the spiropyran motif, and the results presented here may contribute to the development of more useful CN$^-$ receptors.

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Supporting Information Available: Experimental details and supplementary data (Figures S1−S9, Table S1, and Cartesian coordinates for compounds). This material is available free of charge via the Internet at http://pubs.acs.org.

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(18) Cottone, G.; Noto, R.; Manna, G. L.; Fornili, S. L. *Chem. Phys. Lett.* **2000**, *319*, 51–59.

(19) Suzuki, T.; Oda, N.; Tanaka, T.; Shinozaki, H. *J. Mater. Chem.* **2006**, *16*, 1803–1807.

(20) Compund **1** allows selective CN$^-$ detection even at neutral pH, but the sensitivity decreases significantly. This is because the protonation of CN$^-$ (pK_a (HCN) = 9.2) at neutral pH suppresses the nucleophilic addition of CN$^-$ to **1**; the association constant between **1** and CN$^-$ under UV irradiation obtained at pH 7.3 (HEPES) is 92 M^{-1}, whereas the constant obtained at pH 9.3 is 9.8×10^3 M^{-1}.